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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,476	09/27/2001	Michael Mendez	40977	5080

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EXAMINER	
SANDALS, WILLIAM O	
ART UNIT	**PAPER NUMBER**
1636	

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14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/762,476	Mendez et al.
Examiner	**Art Unit**
William Sandals	1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 31, 2003*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above, claim(s) *14-19, 23-26, and 33-47* is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-13, 20-22, and 27-32* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Sep 27, 2001* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examine

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 8
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I, claims 1-13, 20-22 and 27-32, in Paper No. 11, filed January 31, 2003 is acknowledged.

2. Claims 14-19, 23-26 and 33-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups II-IV, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

The traversal is on the grounds that the amendments to claims 1-6 it would not be an undue burden to examine claims 1-34 because all those claims relate to vectors that can shuttle between bacteria and yeast.

This is not found persuasive because, while the amendments have altered some of the limitations of the claims, there are still fundamental differences between the vectors of Group I and Group II. Group II, claims 14-19, 23-26, 33 and 34 is drawn to a vector with a centromere and a telomere. These elements are unique and provide the basis for a group of vector known as artificial chromosomes, which are biologically, physically, biochemically and patentably distinct from the bacteria/yeast shuttle plasmids of Group I.

Applicants have further traversed the restriction on the grounds that the vectors rely upon homologous recombination, and that the elements framing the insert can either be separate or part of a circle.

This is not found persuasive because the limitations of homologous recombination and the elements framing the insert which can either be separate or part of a circle do not distinguish the restriction of the groups, and as such do not affect the restriction requirement.

The requirement is still deemed proper and is therefore made FINAL.

Status of the Claims

3. Claims 1-47 are pending. Claims 1-13, 20-22 and 27-32 are examined in this office action. Claims 14-19, 23-26 and 33-47 are withdrawn from consideration as being drawn to non-elected Groups II-IV. Claims 1-6 have been amended in Paper No. 11.

4. Claim 2 stands objected to for informalities.

5. Claims 20-22 stand rejected under 35 U.S.C. 112, second paragraph.

6. Claims 1, 2, 4, 6, 20-22 and 27-31 stand rejected under 35 U.S.C. 102(b) as being anticipated by Brunelli et al.

7. Claims 1, 6-8, 20-22 and 27-32 stand rejected under 35 U.S.C. 102(b) as being anticipated by US 5,646,037 (Buxton).

8. Claims 1-13, 20-22 and 27-32 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Brunelli et al. in view of US 2002/01760076 A1 (Dymecki) and further in view of US 5,646,037 (Buxton), Liu et al., and US 2001/0014476 A1 (Crouzet et al.).

Claim Objections

9. Claim 2 is objected to because of the following informalities: The last word in claim 2 is "sit", which is a typographical error, and should read "site". Appropriate correction is required.

Claim Rejections - 35 USC § 112

10.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claim 20 recites the limitation "said cloning system" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 1, 2, 4, 6, 20-22 and 27-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Brunelli et al.

Brunelli et al. teach at the abstract and figure 1, vectors comprising a first portion (arm) having a first selectable marker and a first lox site (first cyclization element) and a second portion (arm) having a second selectable marker and a second lox site (second cyclization element). The vectors comprise an origin of replication as recited in claim 1. The vectors comprise a rare restriction endonuclease recognition site (not 1) on each arm as recited in claim 2. The vectors comprise a target sequence (see page 1313, library construction). The vectors are used in bacterial (*E. coli*) and yeast (*S. cerevisiae*) host cells as recited in claims 20-22 and 27-31 (see the abstract and introduction and page 1314, column 1, lines 32-48). The vectors also contain polylinkers to allow the insertion of heterologous DNA (see the abstract and introduction).

15. Claims 1, 6-8, 20-22 and 27-32 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,646,037 (Buxton).

Buxton teaches at the figures and columns 3-8, vectors comprising a first portion (arm) having a first selectable marker and a first FRT site (first cyclization element) and a second portion (arm) having a second selectable marker and a second FRT site (second cyclization element). The vectors comprise an origin of replication as recited in claim 1. The vectors comprise a target sequence which may be a DNA virus (hepatitis virus) (see column 4, lines 28-68). The vectors are used in bacterial (*E. coli*) and yeast (*S. cerevisiae*) host cells as recited in

claims 20-22 and 27-32 (see column 6, lines 6-44). The target sequence may be inserted into the vector by homologous recombination (see column 2, line 61 to column 3, line 10).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 1-6, 20-22 and 27-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brunelli et al. in view of US 2002/0170076 A1 (Dymecki).

The claims are drawn to vectors comprising a first arm having a first selectable marker and a first cyclization element and a second arm having a second selectable marker and a second cyclization element. The vectors comprise at least one origin of replication. The vectors comprise a rare restriction endonuclease recognition site on each arm as recited in claim 2. The vectors comprise a polylinker on each arm as recited in claim 3. The vectors comprise a LOX site cyclization element on each arm as recited in claim 4. The vectors comprise a sequence homologous to the 5' end of a target nucleic acid on the first arm, and a sequence homologous to the 3' end of a target nucleic acid on the second arm as recited in claim 5. The vectors comprise a target sequence as recited in claim 6. The vectors are used in bacterial (*E. coli*) and yeast (*S. cerevisiae*) host cells as recited in claims 20-22 and 27-31.

Brunelli et al. teach at the abstract and figure 1, vectors comprising a first portion (arm) having a first selectable marker and a first lox site (first cyclization element) and a second portion (arm) having a second selectable marker and a second lox site (second cyclization element). The vectors comprise an origin of replication as recited in claim 1. The vectors comprise a rare restriction endonuclease recognition site (not 1) on each arm as recited in claim 2. The vectors comprise a target sequence (see page 1313, library construction). The vectors are used in bacterial (*E. coli*) and yeast (*S. cerevisiae*) host cells as recited in claims 20-22 and 27-31 (see the abstract and introduction and page 1314, column 1, lines 32-48). The vectors also contain polylinkers to allow the insertion of heterologous DNA (see the abstract and introduction).

Brunelli et al. do not teach that each arm of the vector contains a polylinker.

Dymecki teaches at the figures, the abstract, brief summary, paragraph 0032, paragraph 0123, paragraph 0130 and paragraph 0141, vectors comprising a first arm having a first selectable marker and a first cyclization element (FRT) and a second arm having a second selectable marker and a second cyclization element (FRT). Dymecki teaches the alternate use of FRT or LOX (cyclization elements) at paragraph. The vectors comprise a rare restriction endonuclease recognition site (Not 1) on one arm (see the figures and paragraph 0032). The vectors comprise a polylinker on each arm as recited in claim 3 (see the figures and paragraphs 0118 & 0123). The target sequence may be inserted into the vector by homologous recombination as recited in claim 5 (see paragraph 0030). The vectors comprise a target

sequence as recited in claim 6 (see the figures and paragraphs 0139-0145). The target sequence may comprise an HSV thymidine kinase gene (see paragraph 0050). The vectors may be used in bacterial (*E. coli*) and eukaryotic host cells as recited in claims 20-22 and 27-31 (see examples 1 and 2). The insertion of the target sequences by homologous recombination as described in paragraph 0030 does not recite the 5' to 3' orientation of the target sequences with respect to the vector sequences, however, inspection of the figures demonstrates that the orientation of the target sequences is consistent with the requirements of claim 5, in that the vectors comprise a sequence homologous to the 5' end of a target nucleic acid on the first arm, and a sequence homologous to the 3' end of a target nucleic acid on the second arm.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the vectors with lox sites (cyclization elements) and selectable markers on each arm of Brunelli et al. with the vectors with FRT sites (cyclization elements) and selectable markers with polylinkers added on each arm, as taught by Dymecki, for the expected benefit of facilitating the insertion of various desired DNA sequences at the polylinkers on each arm of the vector of Brunelli et al. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Brunelli et al. and Dymecki who demonstrate the use of vectors with lox sites and selectable markers on each arm.

18. Claims 1-9, 20-22 and 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brunelli et al. and Dymecki as applied to claims 1-4, 6, 20-22 and 27-31 above, and further in view of US 5,646,037 (Buxton).

The claims are drawn to the invention as described above and where the target sequences comprise a virus, which may be a DNA virus as recited in claims 7-9.

Brunelli et al. and Dymecki teach the invention as described above. Dymecki teaches the incorporation of herpesvirus DNA (HSV thymidine kinase) into the region of DNA to be delivered by the plasmid pFRTZ, which corresponds to the claimed composition of claim 9 (see for example paragraphs 0050 & 0141).

Brunelli et al. and Dymecki do not specifically teach that the target sequence is a virus, which may be a DNA virus.

Buxton teaches that the vectors comprise a target sequence which may be a DNA virus (hepatitis virus) (see column 4, lines 28-68). The vectors are used in bacterial (*E. coli*) and yeast (*S. cerevisiae*) host cells as recited in claims 20-22 and 27-32 (see column 6, lines 6-44).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the vectors with lox sites and selectable markers on each arm as taught by Brunelli et al. with the vectors with lox sites and selectable markers on each arm by including the target sequences which are from a DNA virus, as taught by Buxton, for the expected benefit of making the vector useful for the delivery of a wide variety of polypeptides encoded by heterologous genes from DNA viruses. Further, a person of ordinary skill in the art would have

had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Brunelli et al., Dymecki and Buxton who demonstrate the use of vectors with lox sites and selectable markers on each arm.

19. Claims 1-11, 20-22 and 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brunelli et al., Dymecki and Buxton as applied to claims 1-9, 20-22 and 27-32 above, and further in view of Liu et al.

The claims are drawn to the invention as described above and where the virus is an RNA virus, which may be a retrovirus, as recited in claims 10-11.

Brunelli et al., Dymecki and Buxton teach the invention as described above.

Brunelli et al., Dymecki and Buxton do not teach that the virus is an RNA virus, which may be a retrovirus.

Liu et al. teach a vector with a LOX site, a selectable marker, an origin of replication and a target DNA insert which may comprise sequences from a retrovirus (RNA virus) as recited in claims 10 and 11 (see Liu et al. at the abstract, page 1301, column 2, page 1304, column 2 and figures 1 & 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the vectors with lox sites and selectable markers on each arm, as taught by Brunelli et al., with the vector with a LOX site, a selectable marker, an origin of replication and a target DNA insert which may comprise sequences from a retrovirus (RNA virus), as taught by

Liu et al., for the expected benefit of making a construct suitable for expression of desired sequences from a retrovirus. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Brunelli et al., Dymecki, Buxton and Liu et al. who demonstrate the use of vectors with lox sites and selectable markers to express desired sequences.

20. Claims 1-13, 20-22 and 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brunelli et al., Dymecki, Buxton and Liu et al. as applied to claims 1-11, 20-22 and 27-32 above, and further in view of US 2001/0014476 A1 (Crouzet et al.).

The claims are drawn to the invention as described above and where the RNA virus is a lentivirus, which may be HIV as recited in claims 12 and 13.

Brunelli et al., Dymecki, Buxton and Liu et al. teach the invention as described above.

Brunelli et al., Dymecki, Buxton and Liu et al. do not teach that the RNA virus is a lentivirus, which may be HIV.

Crouzet et al. teach at paragraphs 0013, 0015-0019, 0035-0037, 0064 and claims 1-15, a vector comprising a cyclization element (Xer), selectable markers, an origin of replication and a desired insert (target) nucleic acid sequence, where the desired nucleic acid sequence is from HIV.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the vectors with lox sites (cyclization elements) and selectable markers on each

arm, as taught by Brunelli et al., with the vector comprising a cyclization element (Xer), selectable markers, an origin of replication and a desired insert (target) HIV sequence, as taught by Crouzet et al. for the expected benefit that the nucleic acid sequence of interest encodes an HIV gene suitable for producing vaccines or making an antigenic peptide for generating an immune response in an animal. Further, a person of ordinary skill in the art would have had a reasonable expectation of success in the producing the instant claimed invention given the teachings of Brunelli et al., Dymecki, Buxton, Liu et al. and Crouzet et al. who demonstrate the use of vectors with lox sites and selectable markers to express desired sequences.

Conclusion

21. Certain papers related to this application are ***welcomed*** to be submitted to Art Unit 1636 by facsimile transmission. The FAX numbers are (703) 308-4242 and 305-3014. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative, and the FAX receipt from your FAX machine is proof of delivery. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications should be directed to Dr. William Sandals whose telephone number is (703) 305-1982. The examiner normally can be reached Monday through Thursday from 8:30 AM to 7:00 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached at (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Tech Center customer service center at telephone number (703) 308-0198.

William Sandals, Ph.D.

Examiner

April 18, 2003

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
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